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Submission date: 20-Sep-2018 10:08AM (UTC+0800)
Submission ID: 1005036390
File name: Bukti_C-3.pdf (1.15M)
Word count: 8531
Character count: 44991

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Review

Chemical Constituents and Bioactivities of Several Indonesian Plants Typically Used in Jamu

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Received December 6, 2017

This article reviews the chemical constituents and bioactivities of several Indonesian plants typically used in Jamu prescriptions in Indonesia. Jamu is Indonesia traditional medicine: it consists of either a single ingredient or a mixture of several medicinal plants. One plant family always used in Jamu is Zingiberaceae (ginger), such as *Curcuma domestica/C. longa*, *C. xanthorrhizae*, *C. heyneana*, *C. zedoaria*, *C. aeruginosa*, *Zingiber aromaticum*, *Alpinia galanga*. We also report other commonly used plant families such as *Justicia gendarussa* and *Cassia siamea*, whose activities have been extensively explored by our department.

Key words bioactive; Zingiberaceae; *Justicia gendarussa*; *Cassia siamea*

1. Introduction

Indonesia is home to the world's greatest biodiversity, with around 143 million hectares of rainforest (Indonesia Country Study on Biodiversity). The hundreds of ethnic groups who live in and around the forests and villages have each developed their own specific traditional medicines. These traditional medicines are found in Bali, Madura, Solo, Surakarta, Yogyakarta, Borneo, C[illegible]es, Papua, *etc*. Before modern healthcare systems were introduced to the Indonesian people, medicinal plants had been the only form of medici[illegible]sed to treat and cure illness. Old stories and methods of healing have been transferred from generation to generation, and have been practiced for hundreds of years using available medicinal plants. Information [illegible]m the older generation, or based on empirical evidence, were the only reasons for using specific plants as a remedy for a specific symptom or illness.

Indonesia, a country in Southeast Asia, has more than 30000 species of medicinal plants. It is estimated that among these, 6000 species have various biological activities, and 1000 species are commonly used in Indonesia traditional medicines or Jamu.[1] Jamu co[illegible]sts of either a single botanical ingredient or the mixture of medicinal plants, and is used for the prevention or treatment of disease, including diseases passed genetically from generation to generation. Many medicinal plants provide relief of symptoms comparable to the relief obtained from traditional medicine formulations.

Zingiberaceae is an essential plant used in the preparation of many beneficial products such as food, spices, herbal medicines, dyes, perfume, and beauty treatments[2]; it is also a frequent[illegible]redient in Jamu. This important group of rhizomatous medicinal and aromatic plants is distinguished by the existence of volatile oils and oleoresins, and is widely distributed in Indonesia. Volatile oils or essential oils consist of numerous complex terpenoid mixtures which are widely used in a variety of therapeutic activities: antimicrobial, antiarthritic, antioxidant, anticancer, antiinflammatory, antidiabetic, anti-human immunodeficiency virus (HIV), n[illegible]protective, larvicidal *etc*.[3–10] The most essential genera of Zingiberaceae are *Curcuma*, *Kaempferia*, *Zingiber*, *Alpinia*, *Elettaria* and *Costus*.[11] Herein we discuss several genera of Zingiberaceae.

2. *Curcuma domestica/Curcuma longa*

Curcuma domestica (syn. *Curcuma longa*) is best known by its common name, turmeric, and belongs to the ginger family, Z[illegible]iberaceae. The rhizome of this plant has traditionally been used as a coloring agent in foods, as a food additive, and in cosmetics.[12,13] Li *et al*. reported that this plant contains at least 235 compounds: amo[illegible]these, they identified primarily phenolics and terpenoids, including 2[illegible]diarylheptanoids and diarylpentanoids, 8 phenylpropene, 68 monoterpenes, 109 sesquiterpenes, 5 diterpenes, 3 triterpenoids, 4 sterols, 2 alkaloids, and 14 other compounds.[14]

The methanol extract of *Curcuma domestic*[illegible], rhizome led to 3 new curcuminoids, [curcumalongin A (**1**), B (**2**) and C (**3**)], along with the kn[illegible] demethoxycurcumin (**4**),[15] bisdemethoxycurcumin (**5**),[15] 1,7-bis(3,4-dihydroxyphenyl)-1,6-heptadiene-3,[illegible]one (**6**),[16] 1-(4-hydroxyphenyl)-7-(3,4-dihydroxyphenyl)-1,6-heptadiene-3,5-dione (**7**),[17] 1-(4-hydroxy-3-methoxyphe[illegible])-7-(3,4-dihydroxyphenyl)-1,6-heptadiene-3,5-[illegible]ne (**8**),[17] 1,5-bis(4-hydroxyphenyl[illegible])-4-pentadiene-3-one (**9**),[18] 5-hydroxy-1,7-bis(4-hydroxyphenyl)-4,6-heptadiene-3-one (**10**),[17] 1,5-dihy[illegible]oxy-1,7-bis(4-hydroxyphenyl)-4,6-heptadiene-3-one (**11**),[17] 1,5-dihydroxy-1,7-bis(4-hydroxyl-3-methoxyphenyl)-4,6-heptadiene-3-one (**12**)[17] and curcumin (**13**)[15] (Fig. 1). New curcumalongin **1**–**3** inhibited the effects of H1N1 neuraminida[illegible] (IC_{50}=6.18±0.64 to 40.17±0.79 μg/mL) and H9N2 (IC_{50}=3.77±0.75 to 31.82±1.33 μg/mL). Compounds **4**, **5**, and **13** also significant[illegible]nhibited the effects of H1N1 neuraminidases (wild type (WT)) and oseltamivir-resistant novel H1N1 (H274Y mutant) expressed in 293T cells, with IC_{50} values of

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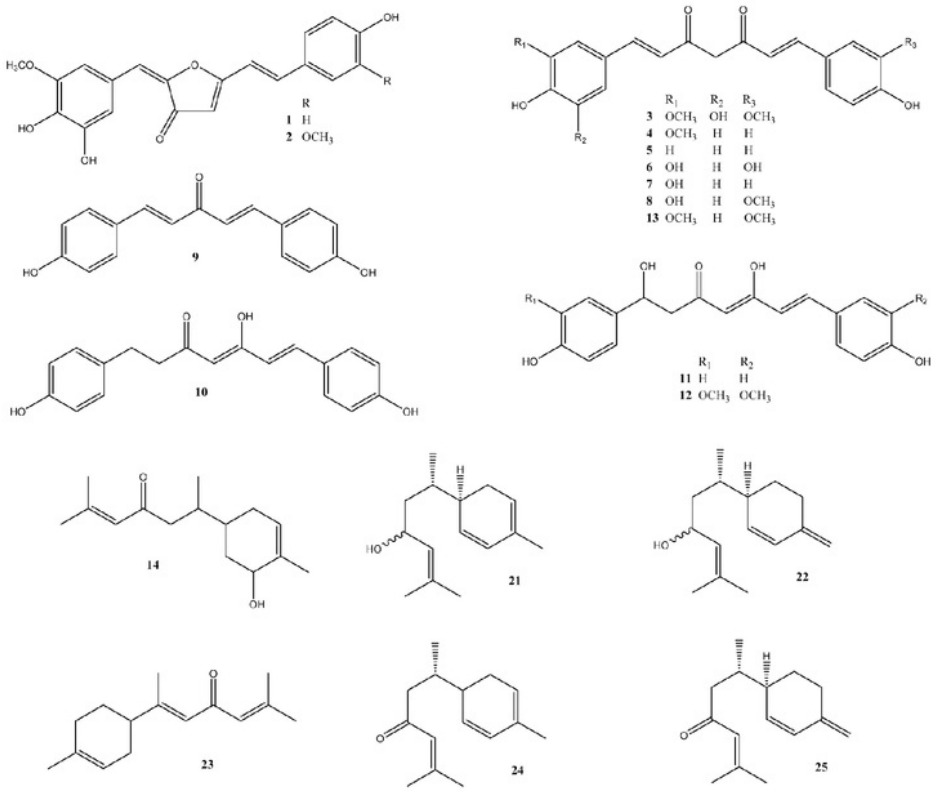

Fig. 1. Structure of Chemical Constituents from *Curcuma domestica* Rhizome

4.36±0.57, 6.95±0.92, and 3.46±0.27 μg/mL, respectively. Their curcuminoids show promise as supplemental molecules for use in the prevention and treatment of influenza virus diseases.[19]

Five new bisabolane-type sesquiterpene curcuminoids, such as bisabocurcumin (**14**)[20] (Fig. 1), turmerone A (**15**),[21] B (**16**),[21] C (**17**)[21] and Q (**18**),[22] along with known **4**, **5**, **13**, (1*E*,4*E*)-1,5-bis(4-hydroxy-3-methoxyphenyl)-penta-1,4-dien-3-one (**19**), and (1*E*,4*E*)-1-(4-hydroxy-3-methoxyphenyl)-5-(4-hydroxy phenyl-)-penta-1,4-dien-3-one (**20**), were isolated from the rhizome.[22] Bisabolane sesquiterpenoids exhibit the production of nitric oxide (NO) induced by lipopolysaccharides (LPS) in RAW264.7 macrophages assays.[22] The turmeric rhizome from Malaysia was obtained a new bisabolane-type sesquiterpenoid, bisacurol B (**21**), along with **4**, **5**, **13**, bisacurol (**22**), *E*-α-atlantone (**23**),[23] ar-turmerone (**24**),[24] and β-turmerone (**25**).[25]

From volatile compounds inside this plant, we identified 28 compounds: **23** (0.5%), **24** (12.9%), **25** (16.0%), α-turmerone (**26**, 42.6%), α-phellandrene (**27**, 6.5%), 1,8-cineole (**28**, 3.2%), α-zingiberene (**29**, 1.9%), terpinolene (**30**, 1.4%), β-sesquiphellandrene (**31**, 1.4%), ar-turmerol (**32**, 1.1%), curzerenone (**33**, 1.1%), ar-curcumene (**34**, 1.0%), *p*-cymene (**35**, 0.9%), epi-α-cadinol (**36**, 0.8%), β-phellandrene (**37**, 0.6%), γ-terpinene (**38**, 0.5%), β-atlantol (**39**, 0.5%), γ-eudesmol (**40**, 0.5%), germacrone (**41**, 0.5%), (*E*)-β-farnesene (**42**, 0.4%), α-terpinene (**43**, 0.3%), α-terpineol (**44**, 0.3%), β-bisabolene (**45**, 0.3%), β-eudesmol (**46**, 0.3%), (6*R*,7*R*)-bisabolone (**47**, 0.3%), α-pinene (**48**, 0.2%), myrcene (**49**, 0.2%), and β-caryophyllene (**50**, 0.2%),[26] cyclocurcumin (**51**), cyclodemethoxycurcumin (**52**) and cyclobisdemethoxycurcumin (**53**).[27]

Curcumin (**13**), a main constituent of this plant, is useful as an anticarcinogenic by inducing apoptosis and reducing cell cycle progression, thus preventing cancerous cell growth. It suppresses carcinogenesis in the liver, kidney, colon, and breast *in vitro* and *in vivo*. In human clinical trials, up to 10 g/d was orally consumed. Therefore it is suggested that curcumin is a promising component in the prevention and treatment of cancer. The antioxidant activities of aqueous extracts of this plant exhibited higher IC_{50} values (8.33 μg/mL) compared with those of curcumin alone (7.85 mg/mL).[28]

3. *Curcuma xanthorrhiza*

Curcuma xanthorrhiza, also known as Javanese turmeric or temulawak, is a ginger-like plant of the Zingiberaceae family, and is found throughout Southeast Asia. It is effective in treating skin eruptions, fever, diarrhea, stomach diseases and constipation. Analysis of the volatile oil of this plant rhizome using GC/MS showed predominantly monoterpenes (88.53%) and sesquiterpenes (2.72%), including **13** (5.85%), **30** (24.86%) and *p*-cymen-7-ol (**54**, 12.17%). Helen *et al.*[29] reported that xanthorrhizol (**55**, 64.38%) was determined to be a major compound, followed by **48** (1.93%), camphene (**56**, 8.27%), and α-curcumene (**57**, 41.40%). Jarikasem *et al.*[30] reported that **28** (37.58%) and **33** (13.70%) were the highest proportion components found in this plant part.[31] Other compounds include monoterpen **42** (0.29%), isoborneol (**58**, 0.04%), camphor (**59**, 0.21%), *E*-elemene (**60**, 4.60%), and *trans*-caryophyllene (**61**,

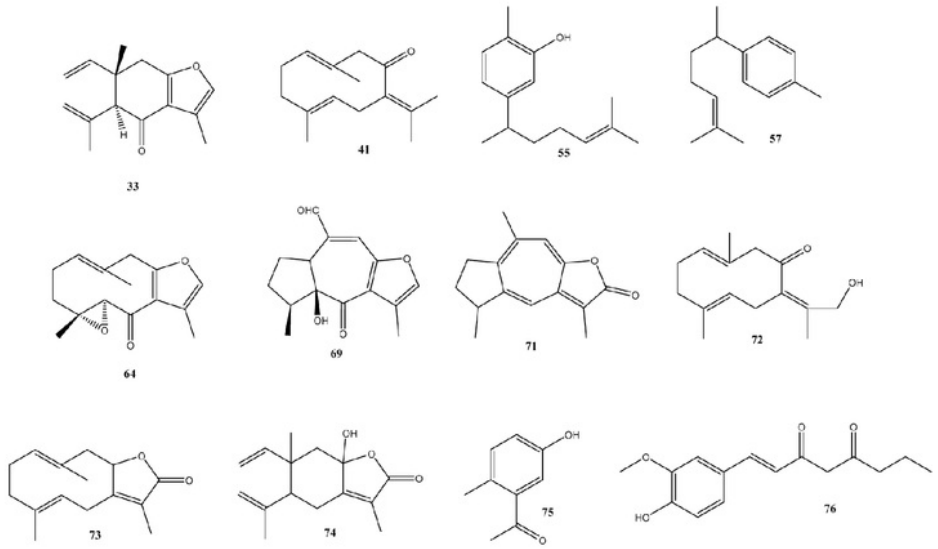

Fig. 2. Structure of Chemical Constituents from *Curcuma xanthorrhiza* Rhizome

3.48%), as well as two new phenolic diarylheptanoids, 5-hydroxy-7-(4-hydroxyphenyl)-1-phenyl(1*E*)-1-heptene (**62**) and 7-(3,4-dihydroxyphenyl)-5-hydroxy-1-phenyl-(1*E*)-1-heptene (**63**). Compounds **62** and **63** displayed significant hypolipidemic action by inhibiting hepatic triglyceride secretion.[32]

Hexane extracts of this plant afforded **41**, **57**, zederone (**64**), oxycurcumenol epoxide (**65**), isocurcumenol (**66**) and curcumenol (**67**), while dichloromethane extracts gave **17**, **55** and stigmasterol (**68**). A non-polar extract showed high larvicidal toxicity, with an a lethal concentration (LC_{50}) value of 26.4–34.9 μg/mL. Compounds **65**, **67** and **66** displayed moderate cytotoxic activity, with IC_{50} values of 11.9, 12.6 and 13.3 μg/mL, respectively, whereas **13** presented the strongest inhibitory activity, with an IC_{50} value of 9.1 μg/mL.[31]

Two novel Guaiane-type sesquiterpenes, zedoaraldehyde (**69**) and zedoardiol (**70**), together with known **41**, **57**, gweicurculactone (**71**), 13-hydroxygermacrone (**72**),[33] gelchomanolide (**73**),[34] 8β-hydroxy-isogermafurenolide (**74**),[35] 3-hydroxy-6-methylacetophenone (**75**),[36] and dehydro-6-gingerdione (**76**) were isolated from this plant (Fig. 2). Among them, **41**, **69**, and **57** inhibited acetylcholinesterase (AChE) activities using a TLC bioautography assay, with minimum inhibitory quantity (MIQ) values of 6, 4, and 1 mg, respectively. Also **75**, **69**, **72**, and **41** enhanced SIRT1 expression by 1.27-, 1.37-, 1.71-, and 1.73-fold, respectively.[37,38]

From the flower bracts of this plant we obtained **55** (16.13%), **57** (15.12%), **58** (0.04%), **59** (0.21%), **60** (4.60%), **61** (0.29%), and **62** (3.48%). It was shown that **13** and **57** significantly inhibited *Propionibacterium acnes*, with minimum inhibition concentration (MIC) values of 0.50 and 2.00 mg/mL and minimum bactericidal concentration (MBC) values of 1.00 and >2.00 mg/mL, respectively. These two also inhibited lipase and and worked as antioxidants at 9.1±1.1 and 57.0±4.5 mg/mL, respectively, with an IC_{50} value of >16.7 mg/mL.[39]

The ethanol extract of *C. xanthorrhiza* inhibited uridine diphosphate glucuronosyltransferase (UGT), UGT1A1 and UGT2B7 activity, with IC_{50} values of 279.74±16.33, 9.59–22.76 and 110.71–526.65 μg/mL, respectively. The ethanol and aqueous extracts inhibited glutathione *S*-transferase (GST) and GST Pi-1 activities with IC_{50} values of 255.0±13.06 and 580.8±18.56 μg/mL, respectively. Xanthorrhizol (**55**), a main compound of Java turmeric, was the better inhibitor of UGT1A1 (IC_{50} of 11.30±0.27 μM) as compared to the others.[40] Treatment with **55** at a dose of 10 or 25 mg/kg/d significantly reduced fasting and postprandial blood glucose levels in high fat diet (HFD)-induced obese mice. Treatment with **55** lowered levels of insulin, glucose, free fatty acid (FFA), and triglyceride (TG) in serum, and both the epididymal fat pad and adipocyte size were reduced by high doses of **55** (26.6 and 20.1%). **55** also inhibited the growth of fatty liver by reducing liver fat accumulation. Furthermore, **55** significantly suppressed inflammatory cytokine production, such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), interleukin-1β (IL-1β), and C-reactive protein (CRP) in adipose tissue (27.8–82.7%), liver (43.9–84.7%), and muscle (65.2–92.5%). This suggests the potential use of **55** as a powerful antidiabetic agent for type II diabetic therapy.[41]

4. *Curcuma heyneana*

Curcuma heyneana ('temu giring') is a form of Zingiberaceae traditionally used in Malaysia and Indonesia as an anthelmintic, in skin scrubs and to heal wounds. It contains *ca.* 0.43% oil, classified as sesquiterpenes (87.3%), diterpenes (4.8%), and monoterpenes (3.0%). Its sesquiterpenes are **4**, **13**, **28**, **41**, **46**, **48**, **50**, **56**, **58**, **59**, **65**, **66**, **67**, 1(10),4-diepoxygermacrone (**77**), heyneanone A (**78**), B (**79**), C (**80**), D (**81**), dehydrocurdione (**82**), procurcumenol (**83**), curcumenone (**84**), curcumanolide A (**85**), B (**86**), C (**87**), D (**88**), β-pinene (**89**), β-gueyunen (**90**), β-cadinen (**91**), elemol (**92**), humuladion (**93**), curcumandiaerugidiol (**94**), zerumin A (**95**), zerumbone (**96**), zedoarondiol (**97**), 4,10-epizedoarondiol (**98**), 15-hydroxyprocurcumenol (**99**), 12-hydroxycurcumenol (**100**), (*E*)-labda-8(17),12-diene-15,16-dial (**101**), and (*E*)-15,16-bisnorlabda-8(17),11-dien-13-one (**102**), oxycurcumenol (**103**), and aerugidiol (**104**), along with phytosterols **68** and α-sitosterol

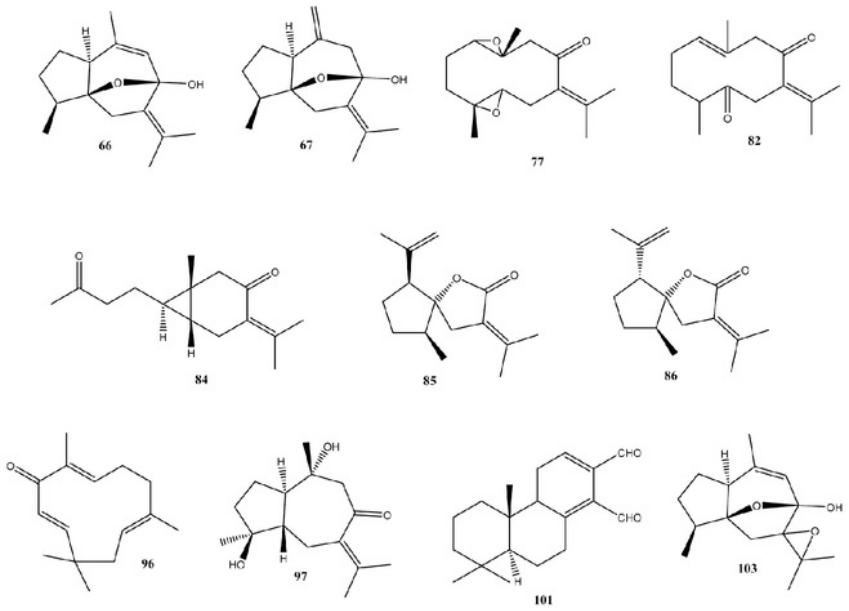

Fig. 3. Structure of Compounds from *Curcuma heyneana*

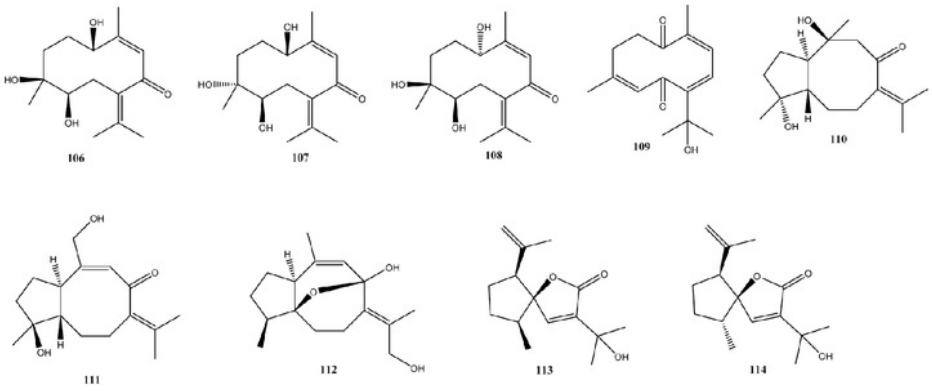

Fig. 4. Several Novel Compounds from *Curcuma heyneana*

(**105**) (Fig. 3). The essential oil composition of a chloroform extract of *Curcuma heyneana* dried rhizome isolated **85** (19.6%), **103** (17.2%), **66** (16.5%), **67** (13.7%), **84** (6.4%), **41** (5.0%) and **101** (4.8%).[42] Antibacterial screening revealed that **84** showed inhibitory activity against *Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, *B. cereus* and *Streptococcus faecalis*, while **101** showed inhibitory activity against *S. aureus*, *B. subtilis*, *P. aeruginosa*, and *Salmonella typhi* with MIC values of 0.05–0.025.[42]

Four novel germacranes, heyneanones A (**106**), B (**107**), C (**108**), and D (**109**), three novel guaianes, 4,10-epizedoarondiol (**110**), 15-hydroxyprocurcumenol (**111**), and 12-hydroxycurcumenol (**112**), and two novel spirolactones, curcumanolides C (**113**) and D (**114**), were found from the rhizomes of *Curcuma heyneana* (Fig. 4). Among the isolated compounds, **83**, **106**, **99**, **108**, **110**, **90**, and **97** inhibited protein tyrosine phosphatase 1B (PTP1B) with IC_{50} values of 45.6, 42.5, 35.7, 35.2, 35.1, 10.4, and 14.7 μM, respectively. PTP1B is an enzyme initiated in significant insulin-targeted organs such as the liver and muscle, and the inhibition or removal of this enzyme initiates insulin signaling and glucose circulation. Thus, modification and inhibition of this phosphatase will create peripheral glucose homeostasis, improve energy expenditure, and decrease weight. Accordingly, the inhibition of this enzyme is a well-validated target for the treatment of type II diabetes and obesity.[43]

The oil of this plant was shown to be quite toxic, with ED_{50} values of 46.61 ppm against brine shrimp and moderate effects against *P. aeruginosa*. **84** showed inhibitory activities toward *S. aureus*, *B. subtilis*, *P. aeruginosa*, *B. cereus* and *S. faecalis*, whereas **101** showed inhibitory activities toward *S. aureus*, *B. subtilis*, *P. aeruginosa*, and *S. typhi*, with MIC values of 0.05–0.025 μg/mL. Compound **50** inhibited *P. aeruginosa* with MIC and MBC values of 15.6 and 31.2 μg/mL, respectively. *S. aureus*, *Escherichia coli*, *S. typhi* and *Vibrio cholerae* (MIC and MBC values of 62.5 μg/mL), and *Enterobacter*

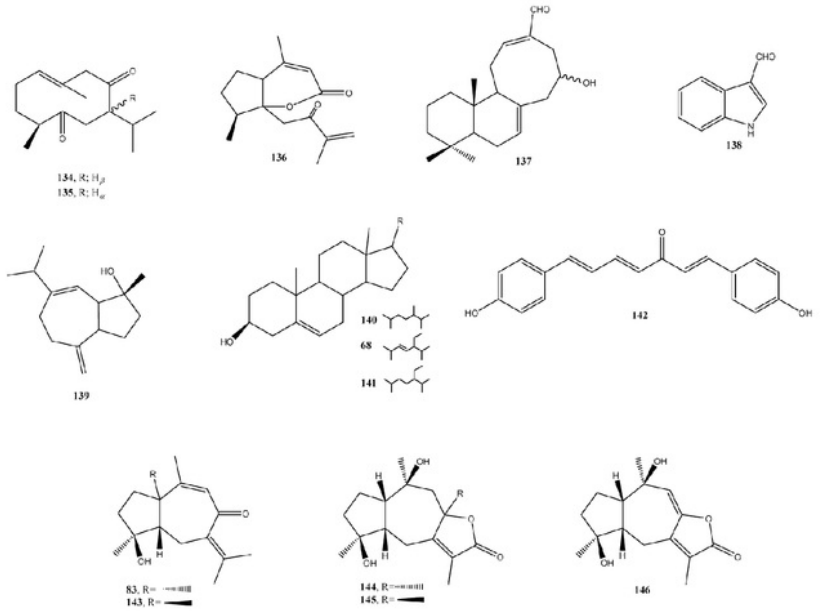

Fig. 5. Structure of Isolated Compounds from *Curcuma zedoaria*

aerogenese and *Shigella dysentriae* (MIC and MBC values of 125 μg/mL). Compound **82** inhibited *B. subtilis* with MIC and MBC values of 31.2 μg/mL, *E. coli* (MIC and MBC value of 62.5 μg/mL), *E. aerogenese*, *P. aeruginosa*, *S. dysentriae*, *V. cholerae* (MIC and MBC value of 125 μg/mL), as well as *S. aureus* and *S. typhi* (MIC and MBC value of 250 μg/mL). It is thus suggested that the chemical components of *C. heyneana* rhizomes have potent antibacterial properties.[44]

Compounds **65**, **67** and **76** were confirmed to exhibit moderate inhibition toward CEM-SS cytotoxic activity, with IC_{50} values of 11.9, 12.6 and 13.3 μg/mL, respectively.[45] Compounds **95**, **102**, **98**, **80**, **68**, **78**, and **83** inhibited protein tyrosine phosphatase 1B (PTP1B) with IC_{50} values of 10.4, 14.7, 35.1, 35.2, 35.7, 44.5, and 45.6 μM, respectively.[46] Compound **97** demonstrated anti-inflammatory activity by the suppression of LPS-stimulated nitric oxide (NO), prostaglandin E_2 (PGE_2), tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), and interleukin-1β (IL-1β) production in RAW264.7 macrophage and mouse peritoneal macrophage cells, dose-dependently.[47] Compound **50** displayed the highest inhibitory activity toward *P. aeruginosa*, with an MIC value of 15.6 μg/mL and MBC value of 31.2 μg/mL. **101** displayed the highest inhibitory activity toward *B. subtilis* with an MIC value of 31.2 μg/mL and MBC value of 31.2 μg/mL. **77** showed weak antibacterial activity.[44]

5. *Curcuma zedoaria*

Curcuma zedoaria is a close relative of *Curcuma longa* (Zingiberaceae), traditionally used to cure stomach ache, toothache, blood stagnation, leucoderma, tuberculosis, enlargement of the spleen, to promote menstruation, as a carminative, expectorant, and diuretic, and to treat cold, infection, vomiting, diarrhea and leucorrhea. Several biological activities of this rhizome have been reported, such as antiinflammatory, antifungal, antiulcer, antimicrobial, hepatoprotective, and antiamoebic.[48]

The 32 terpenoids from this plant, as determined by GC-MS, include **38** (0.08%), **42** (9.22%), **44** (0.41%), **46** (0.65%), **48** (0.66%), **49** (0.23%), **50** (1.33%), **56** (1.21%), **58** (1.29%), **59** (2.86%), **89** (0.63%), sabinene (**115**,0.22%), D-limonene (**116**, 0.75%), eucalyptol (**117**, 9.70%), linalool (**118**, 1.11%), borneol (**119**, 0.25%), 4-terpineol (**120**, 0.24%), δ-elemene (**121**, 1.19%), β-elemene (**122**, 8.06%), γ-elemene (**123**, 2.81%), valencene (**124**, 0.34%), α-caryophyllene (**125**, 0.79%), α-gurjunene (**126**, 0.25%), germacrene (**127**, 1.79%), β-selinene (**128**, 0.76%), curzerene (**129**, 29.36%), δ-cadinene (**130**, 0.22%), aristolene (**131**, 0.33%), β-eudesmene (**132**, 0.09%), β-elemenone (**133**, 0.53%), curdione (**134**, 19.57%) and neocurdione (**135**, 3.08%). Among these, **117**, **59**, **129**, **122**, **123**, **41**, and **135** exerted obvious embryotoxicity *ex vivo*, as well as reproductive toxicity in rats (at 3.90, 1.61, 2.67, 1.87, 16.26, 5.01, 19.70 and 1.63%, respectively).[49]

The dried rhizome of this plant afforded a novel 7,8-*seco*-guaianolide, curcuzedoalide (**136**), together with two known metabolites, curcuminol D (**137**) and indole 3-carbaldehyde (**138**) (Fig. 5). A total of 40 components of volatile oil were identified from this plant respectively; the major ones are **33** (31.6%), **41** (10.8%), **59**, and **67**, as determined by GC-MS.[50] Compound **67** exhibited potent and dose-related analgesic activity using writhing, formalin and capsaicin methods (with ID_{50} values of 2.49 and 12 μmol/kg, respectively).[51]

Based on a bioassay-guided isolation method, the active hexane fraction of a methanol extract of this plant produced **33**, **64**, **68**, **134**, **135**, alismol (**139**), and a mixture of campesterol (**140**) and β-sitosterol (**141**). Compounds **33** and **139** showed cell proliferation inhibition in human cancer cell lines such as MCF-7, Ca Ski, and HCT-116, in a dose-dependent manner (12.5–50 μg/mL). Both of these compounds exhibited typical apoptotic morphology of cancer cells, as observed by an inverted phase contrast microscope and Hoechst 33342/PI

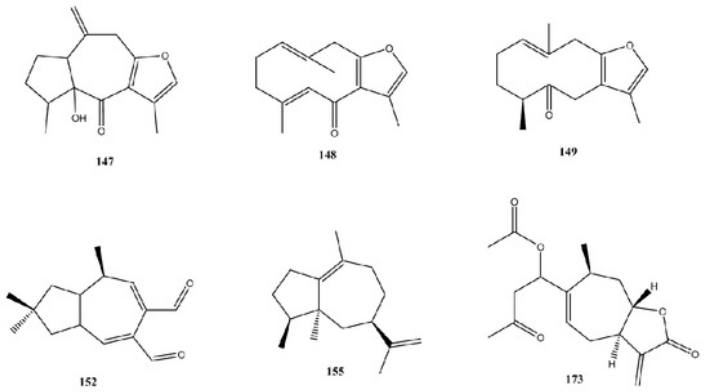

Fig. 6. Isolated Compounds from *Curcuma aeruginosa*

dual-staining test; they encouraged apoptosis through caspase activation.[52]

The EtOAc-soluble fraction of the methanol extract of this rhizome isolated **83**, 1,7-bis(4-hydroxyphenyl)-1,4,6-heptatrien-3-one (**142**), and epicurcumenol (**143**). Compounds **142** and **83** inhibited TNF-α production by LPS-activated macrophages with IC_{50} values of 12.3 and 31.5 mM, respectively.[53] The aqueous extract of the dried bark produced zedoalactones A (**144**), B (**145**) and C (**146**) (Fig. 5), which inhibited bacterial activity with IC_{50} values of 16.5, 1.6 and 4.2 μg/mL, respectively.[54]

The methanol extract of this rhizome showed a cytotoxic effect on AGS cells (IC_{50}: 96.60±4.87 μg/mL), with its strongest effect being the suppression of gastric cancer cell proliferation in a dose-dependent manner [IC_{50} value of 125.11±.77 μM]. It also inhibited AGS human gastric cancer cell viability by caspase-8, -9, -3, and poly(ADP-ribose) polymerase (PARP) activation, which contributed to apoptotic cell death in AGS human gastric cancer cells.[55]

6. *Curcuma aeruginosa*

Curcuma aeruginosa rhizome has traditionally been used to lessen dysmenorrhea, as an analgesic, antipyretic and anti-inflammatory,[56] and to treat cold, cough, asthma, gastrointestinal and uterine maladies. It contains terpenoids, sterols, organic acids, fatty acids and sugars. The sesquiterpenes were identified as **33**, **41**, **64**, **66**, **67**, **82**, **97**, **144**, **145**, zedoalactone (**147**), furanodienone (**148**), and furanogermenone (**149**). They inhibited 5α-reductase, which changes testosterone to dihydrotestosterone (DHT). Among these, **41** showed the highest inhibitory activity (IC_{50}=65.7±4.7%), and displayed an anti-androgenic effect in *in vitro* and *in vivo* assays. It acts as an anti-androgenic against LNCaP cells during testosterone-induced proliferation. Thus, **41** is a potential compound for use in the treatment of androgen-dependent disorders.[57]

The essential oil (94.08%) and oxygenated monoterpenes (5.92%) of this plant were obtained by hydrodistillation of the rhizomes, and were found to include **28** (11.0%), **33** (24.6%), **41** (6.50%), **58** (0.62%), **59** (10.6%), **66** (5.8%), **67** (5.6%), **117** (3.98%), **122** (4.76%), **149** (5.5%), alloaromadendrene oxide-(2) (**150**, 6.3%), cycloisolongifolene, 8,9-dehydro-9-formyl (**151**, 35.29%), dihydrocostunolide (**152**, 22.51%), velleral (**153**, 10.00%), aromadendrene oxide-(2) (**154**, 2.40%), α-bulnesene (**155**, 2.14%), eudesma- 4(14),11-diene (**156**, 1.13%), L-camphor (**157**, 1.32%), cubebene (**158**), xanthinin (**159**), and (*Z*)-3-hexenol (**160**) based on GC and GC/MS[58] (Fig. 6).

Extraction methods revealed quite different results. Extraction by two-phase methanol/chloroform (M/C) led to higher metabolite exposure compared to extraction by methyl *tert*-butyl ether (MTBE). The MTBE extraction yielded 27 compounds, whereas M/C extraction revealed 18 (polar) and 36 (nonpolar) fractions. The major compounds of MTBE extract were determined to be methenolone (**161**, 16.64%), cycloisolongifolene, 8,9-dehydro-9-formyl- (**162**, 15.93%), labd-13-en-15-oic acid, 8,12-epoxy-12-hydroxy-γ-lactone (**163**, 10.77%), propiolic acid, 3-(1-hydroxy)-2 isopropyl-1,5-methyl-cyclohexyl) (**164**, 7.84%), 4-oxo-β-isodamascol (**165**, 5.17%), **152** (3.61%) and *Z*-α-farnesene (**166**, 2.00%). These were detected based on the peak area percentage.

The major compounds of the polar fraction of M/C extraction were recognized as **41** (1.41%), **122** (1.33%), **129** (1.56%), **166** (1.52%), α-D-glucopyranoside,1,3,4,6 tetrakis-*O*-trimethylsilyl (TMS)-β-D-fructofuranosyl 2,3,4,6-tetrakis-*O*-(TMS) (**167**, 38.08%), D-glucose, 2,3,4,5,6-pentakis-*O*-(TMS)-*O*-methyloxime (**168**, 14.61%), D-fructose, 1,3,4,5,6-pentakis-*O*-(TMS)-*O*-methyloxime (**169**, 5.28%), isocitric acid-(TMS) (**170**, 3.06%), oxalic acid,bis-(TMS) ester (**171**, 2.96%), hexadecanoic acid, TMS ester (**172**, 2.16%), citric acid, ethyl ester, tri-TMS (**173**, 1.91%), and butanedioic acid, [(TMS) oxy]-bis(TMS) ester (**174**, 1.14%). In the non-polar extract, the major compounds distinguished are cycloisolongifolene, 8,9-dehydro-9-formyl (**175**, 15.70%), propiolic acid, 3-(1-hydroxy-2-isopropyl-5-methylcyclohexyl) (**176**, 11.09%), stearic acid, TMS ester (**177**, 2.78%), hexadecanoic acid, TMS ester (**178**, 2.33%), and oleic acid, TMS ester (**179**, 1.62%). Therefore, different methods of extraction yielded different compounds.[59]

7. *Zingiber aromaticum*

Z. aromaticum VAHL (Zingiberaceae) is another common Jamu widely used in Indonesia. Its rhizomes, commonly called "Lempuyang wangi," are used to treat cholescystopathy, whooping cough, jaundice, arthritis, anorexia, cold, cholera, dysmenia, malaria, rheumatism, and abdominalgia. This plant has been reported to have the strongest anti carcinogenic activity in the Zingiberaceae family. It has been suggested that the sesquiterpene, zerumbone, contained in this plant also has potential to be promoted as a herbal medicinal products

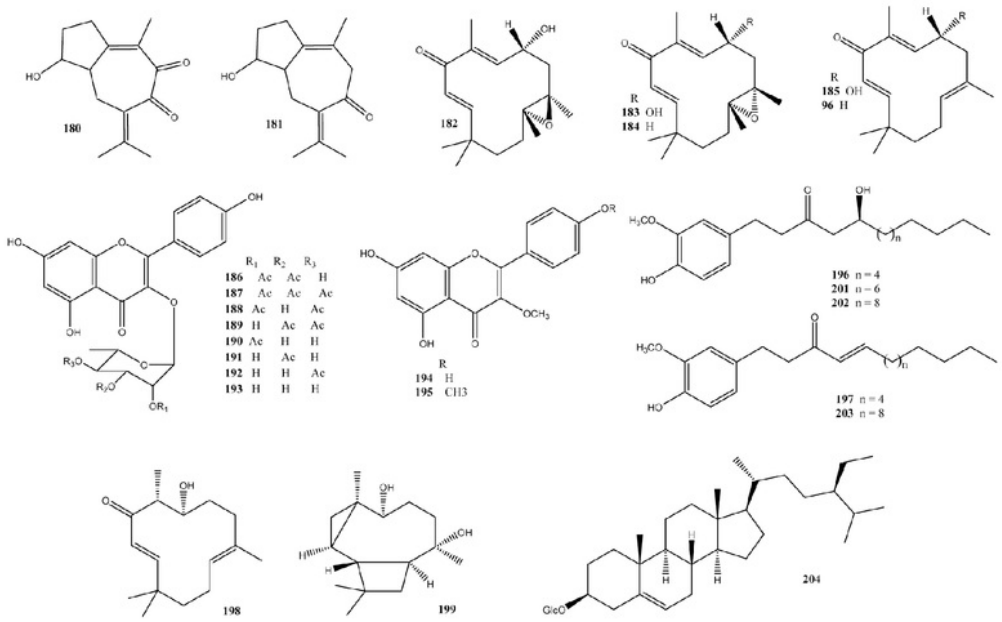

Fig. 7. Structure of Isolated Compounds from *Zingiber aromaticum*

(HMP) anticarcinogenic substance based on its apoptosis induction.[60]

The petroleum ether of this plant rhizome led to 9-oxo-neoprocurcumenol (**180**) and neoprocurcumenol (**181**) using a flash column that inhibited larvicidal activi34. Among the two, **180** demonstrated substantial toxicity on mosquito larvae, with an LC_{50} value of 5.81 ppm ($p<0.01$) and LC_{90} of 9.99 ppm. This compared to **181**, with an LC_{50} value of 13.69 ppm and LC_{90} of 23.92 ppm.[60] 1

Other constituents, including (2*R*,3*S*,5*R*)-2,3-epoxy-6,9-humuladien-5-ol-8-one (**182**), (2*R*,3*R*,5*R*)-2,3-epoxy-6,9-humuladien-5-ol-8-one (**183**), zerumbone epoxide (**184**), (5*R*)-2,6,9-humulatrien-5-ol-8-one (**185**), zerumbone (**96**), kaempferol-3-*O*-(2,3-di-*O*-acetyla-L-rhamnopyranoside) (**186**), kaempferol-3-*O*-(2,3,4-tri-*O*-acetyl-*α*-L-rhamnopyranoside) (**187**), kaempferol-3-*O*-(2,4-di-*O*-acetyl-*α*-L-rhamnopyranoside) (**188**), kaempferol-3-*O*-(3,4-di-*O*-acetyl-*α*-L-rhamnopyranoside) (**189**), kaempferol-3-*O*-(2-*O*-acetyl-*α*-L-rhamnopyranoside) (**190**), kaempferol-3-*O*-(3-*O*-acetyl-*α*-L-rhamnopyranoside) (**191**), kaempferol-3-*O*-(4-*O*-acetyl-*α*-L-rhamnopyranoside) (**192**), kaempferol-3-*O*-*α*-L-rhamnopyranoside (**193**), kaempferol-3-*O*-methyl ether (**194**), kaempferol-3,4-di-*O*-methyl ether (**195**), (*S*)-6-gingerol (**196**), and *trans*-6-shogaol (**197**), were obtained from the methanol fraction of an aqueous extract of this plant (Fig. 7). This fraction exhibited ≥70% inhibition at 25 *μ*g/mL. Compounds **185** (IC_{50}=27.7 *μ*M), **195** (IC_{50}=17.5 *μ*M), and **196** (IC_{50}=28.1 *μ*M) inhibited protein tyrosine phosphatase 1B (PTP1B) activity, and as such may contribute to Type II diabetes and/or obesity therapy and/or prevention.[61]

Th60uman cytochrome (CYP P450) superfamily contributes to the metabolism of a variety of xenobiotics including carcinogens, steroids, eicosanoids and drug therapeutics. Herbal constituents may be absorbed and eliminated by CYP to become nontoxic metabolites, but toxic metabolites are also possible. Kaempferol glycosides and derivatives of **187**, **189**, **194**, and **195** inhibited the metabolism of CYP2D6 enzyme. Additionally, **186**, **187**, and **188**–**195** inhibited the mechanism of CYP3A4 enzyme wherein the inhibition is irreversible, as determined by the catalytic process. Compounds **186**, **187**, and **188**–**195** showed KI values in the range of 2.21–27.01 *μ*M, while the kinact values ranged from 0.23–0.65 min^{-1}. The KI and kinact values of **187** confirm it to be the most potent CYP3A4 inactivator (2.21 *μ*M and 0.45 min^{-1}, respectively),[62] with the most potent metabolism inhibitory activity mediated by CYP3A4 (IC_{50}=14.4 *μ*M), whereas **194** appeared to be the most potent mechanism-based inhibitor of CYP2D6 (IC_{50}=4.63 *μ*M).[63]

From the methanol extract of this plant was isolated a new 2,9-humuladien-6-ol-8-one (**198**) together with **96**, **141**, **184**, **191**, **192**, **193**, **194**, **195**, **197**, tricyclohumuladiol (**199**), (*S*)-6-gingerol (**200**), (*S*)-8-gingerol (**201**), (*S*)-10-gingerol (**202**), *trans*-10-shogaol (**203**), and *β*-sitosterol glucoside (**204**) (Fig. 7). The major constituent of this methanol extract (**96**, 20%) showed CYP inhibitory activity with an IC_{50} value of 21.8 *μ*M. In the group of gingerol derivatives, compound **202**, with a longer side chain, displayed stronger CYP3A4 inhibitory activity than **201** and **200**, suggesting that the length of the side chain may be necessary for the inhibitory activity on CYP3A4.[64]

Zerumbone (**96**) was capa1 of inducing pancreatic carcinoma cell line apoptosis. It induced apoptosis of pancreatic carcinoma (PANC-1) cells as determined by Hoechst 33342, acridine ora42-ethidium bromide (AO/EB), terminal deoxynucleotidyl transferase-mediated deoxyuridine triphosphate nick-end labeling (TUNEL) staining, and caspase-3 activity. In addition, **96** at 30 *μ*M increased reactive oxygen species (ROS) production by about 149% in PANC-1 cells.[65]

8. *Alpinia galanga*

Alpinia galanga WILLD. rhizomes are extensively used

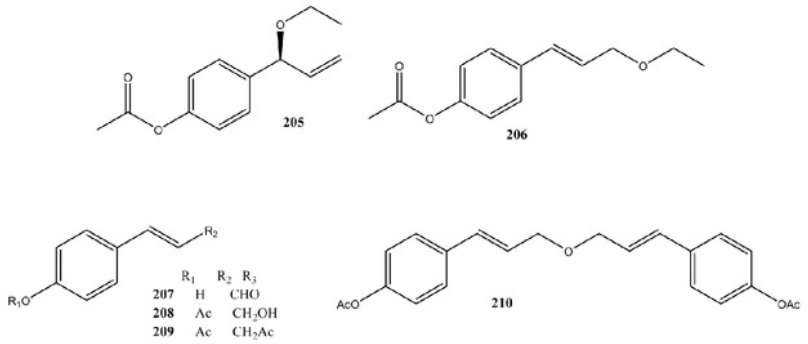

Fig. 8. Structure of Isolated Compounds from the *Alpinia galanga* Rhizome

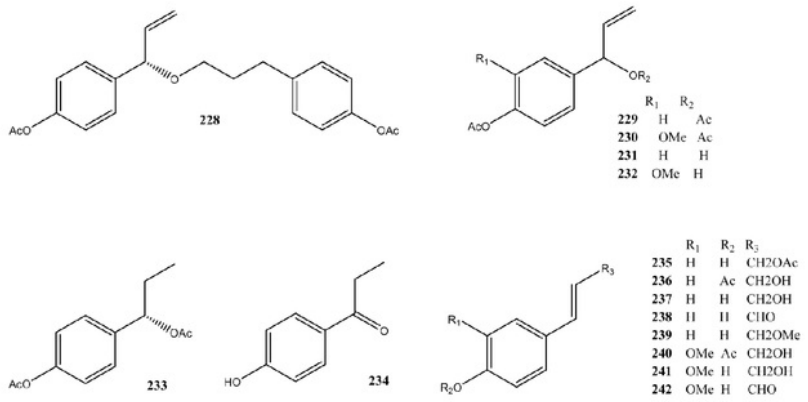

Fig. 9. Chemical Constituents from the Acetone Extract of *Alpinia galanga* Dried Fruit

as a flavoring in traditional foods, and as a stomachic. Two new phenylpropanoids, (*S*)-1′-ethoxy chavicol acetate (**205**) and (*E*)-4-acetoxy cinnamyl ethyl ether (**206**) (Fig. 8), along with (*E*)-4-hydroxylcinnamaldehyde (**207**), 4-acetoxy cinnamyl alcohol (**208**), 4-acetoxy cinnamyl acetate (**209**), 4,4′[(2*E*,2′*E*)-bis(prop-2-ene)-1,1′-oxy]-diphenyl-7,7′-diacetate (**210**), ethyl *trans*-cinnamate (**211**), ethyl 4-methoxy-*trans*-cinnamate (**212**), and 1-acetoxychavicol acetate (**213**) were obtained from this rhizome. Among these, **213** displayed selective inhibitory activity toward A549 human lung adenocarcinoma cells (IC_{50} value of 19.35 μmol/L), whereas other compounds showed no such activity (IC_{50}>20 μmol/L).[66] Compounds **211** and **212** induced GST, a main mechanism for the detoxification of chemical carcinogens, and **213** suppressed chemical and virus-induced tumor initiation and elevation. Although the mechanism is not completely understood, these compounds also inhibited nuclear factor kappa B (NF-κB) activation and NF-κB-regulated gene expression, which may contribute to their capability to increase apoptosis and to inhibit tissue invasion.[66]

From an 80% acetone extract of *Alpinia galanga* rhizome were isolated three new 8-9′ linked neolignans: galanganal (**214**, 0.0048%), galanganols A (**215**, 0.0011%) and B (**216**, 0.0010%), and a novel sesquineolignan, galanganol C (**217**, 0.0015%), together with *p*-hydroxybenzaldehyde, 1′*S*-1′-acetoxychavicol acetate (ACA) (**218**, 1.10%), 1′*S*-1′-acetoxyeugenol acetate (**219**, 0.038%), 1′*S*-1′-hydroxychavicol acetate (**220**, 0.048%), chavicol β-D-glucopyranoside (**221**, 0.023%), methyleugenol (**222**, 0.0006%), *trans*-*p*-hydroxycinnamaldehyde (**223**, 0.028%), *trans*-*p*-coumaryl alcohol (**224**, 0.052%), *trans*-*p*-hydroxycinnamyl acetate (**225**, 0.021%), *trans*-*p*-coumaryl diacetate (**226**, 0.015%), and *p*-hydroxybenzaldehyde (**227**, 0.0047%). Among these, the acetone extracts, compounds **214**, **216**, **217**, **218**, **219**, **223**, **224**, and **226**, showed NO inhibitory activity of LPS-activated mouse peritoneal macrophages [IC_{50} values of 7.3, 68, 88, 33, 2.3, 11, 20, 72 and 19 μM, respectively].[67]

At low dose, ACA or **218** showed Rev transport inhibition by binding to chromosomal region maintenance 1 and accumulating full-length HIV-1 RNA in the nucleus, resulting in an HIV-1 replication block in peripheral blood mononuclear cells. It thus acted synergistically to reduce HIV-1 replication and, as such, represents a novel HIV-1 infection therapy.[68] It has also shown great efficacy in the removal of antibiotic resistance plasmid from *S. typhi* (75%), *P. aeruginosa* (70%), *E. coli* (32%), and vancomycin resistant *Enterococcus* (66%) at an serum inhibitory concentration (SIC) value range of 400–800 μg/mL. Relatively lower plasmid treatment efficacies were detected in *Bacillus cereus* (6%) and *E. coli* harboring plasmid RP4 (7%). As an additional note, the efficacy of antibiotic resistance treatment by a crude acetone extract of *Alpinia galanga* was detected in *S. typhi* and *E. coli*, and was higher compared to 1′-acetoxychavicol acetate.[69]

The acetone extract of *Alpinia galanga* dried fruit inhibited melanogenesis in ecophylline-stimulated murine B16 in melanoma 4A5 cells, with an IC_{50} value of 7.3 μg/mL. The EtOAc

fraction of this extract yielded new galanganol D diacetate (**228**, 0.00292%), together with 10*S*-10-acetoxychavicol acetate (**229**, 0.0977%), 10*S*-10-acetoxyeugenol acetate (**230**, 0.119%), 10*S*-10-hydroxychavicol acetate (**231**, 0.00430%), 10*S*-10-hydroxyeugenol acetate (**232**, 0.00675%), 10*S*-10-acetoxydihydrochavicol acetate (**233**, 0.00028%), 1-(4-hydroxyphenyl)-1-propanone (**234**, 0.00024%), *trans*-*p*-coumaryl acetate (**235**, 0.00140%), *trans*-*p*-acetoxycinnamoyl alcohol (**236**, 0.00162%), *trans*-*p*-coumaryl alcohol (**237**, 0.00168%), *trans*-*p*-coumaryl aldehyde (**238**, 0.00026%), *trans*-*p*-coumaryl alcohol *C*-*O*-methyl ether (**239**, 0.00131%), *trans*-coniferyl alcohol 4-*O*-acetate (**240**, 0.00041%), *trans*-coniferyl alcohol (**241**, 0.00869%), and *trans*-coniferyl aldehyde (**242**, 0.00036%)[70] (Fig. 9).

Compounds **228** and **45** inhibited tyrosinase in mRNA expressions at 10 μM, **229** inhibited the expression of tyrosinase, TRP-1, and TRP-2 mRNA at 10 μM, and **230** inhibited the expression of TRP-1 and TRP-2 mRNA at 3–10 μM. Compounds **228**, **229** and **230** inhibited melanogenesis with IC_{50} values of 2.5, 5.0 and 5.6 μM, respectively. The structure–activity relationship (SAR) melanogenesis activity of phenylpropanoids are (i) compounds with a 4-acetoxy group displaying higher activity than a 4-hydroxy group; (ii) the 3-methoxy group does not influence the activity; (iii) acetylation of the 10-hydroxy moiety increases the activity; and (iv) phenylpropanoid dimers with a 7-*O*-9′-linked neolignan skeleton showed higher activity than their corresponding monomers.[70]

9. *Justicia gendarussa*

Traditionally, *Justicia gendarussa* Burm. f. (Acanthaceae) has been used as a male contraception in Papua. The root, leaves and stem are also used to treat chronic rheumatism, anti-inflammation,[71] arthritis,[72] anticancer,[73] antioxidant,[74] antibacterial,[75] antifungal,[76] antiangiogenesis,[77] and hepatoprotective therapeutic.[78]

The isolation of *Justicia gendarussa* *n*-butanol fraction using preparative HPLC yielded 6,8-di-*C*-*α*-L-arabinocyl-4′,5,7 trihidroxy-flavon or 6,8-di-*C*-*α*-L-arabinocylapigenin (gendarusin A, **243**) as major compound, and methanol fraction using MPLC yielded 6,8-di-*C*-*α*-L-arabinopyranocyl-4′,5,7-trihidroxy-8-*C*-*β*-D-cylopyranocylflavone or 6-*C*-*α*-L-arabinocyl-8-*C*-*β*-D-ylocilapigenin (gendarusin B, **244**) as minor compound, as well as **243**.[79] New alkaloids from the leaves of this plant were isolated as justidrusamides A–D (**245**–**248**) containing 2-aminobenzyl alcohol, succinic acid, and 2,3-dihydroxy-2-(1-hydroxyethyl)butanoic acid frames[80] (Fig. 10). A water decoction of this plant, containing 2-aminobenzyl derivatives and flavonoids, has been compared to the standardized extract used in clinical trials. The comparison showed that the standardized extract used in clinical trials contains primarily **243**, whereas 2-aminobenzyl derivatives were expressively removed by the standardization process. Comparison of various *J. gendarussa* collected from different regions in Indonesia was valuable in selecting the best quality of plant material, containing a higher content of gendarusin A.[81]

Methanol extracts of mature and young leaves of *Justicia gendarusa* from 4 regions in Malaysia were found to contain naringenin (**249**) and kaempferol (**250**). These were identified using gas chromatography-flame ionization detector (GC-FID) analysis. The highest concentrations of **249** and **250** were recorded in mature leaves from the Bukudai and Muar regions, at 507.692 and 1226.964 mg/kg, respectively. Data analysis showed that naringenin content was directly proportional to the amount of kaempferol in the leaf extracts. Our study suggests that geographical variations among plant samples, as well as the physiological stage of organ parts, may contribute to variations in flavonoid concentration in a plant species.[82]

The main content in the polar fraction is **243**, together with **245**–**248**, and **250**. Compound **243** inhibited HIV type-1 reverse transcriptase, and showed the strongest activity (3.6×10^6) at 793 ppm against human plasma HIV, with an IC_{50} value of 235.3 ppm. The 70% ethanol fraction contained 1.4% of **243.** In clinical trials, a bioavailability test in plasma or blood serum from volunteers detected **243** by HPLC; it also appeared in ejaculate and urine from volunteers. Compounds **243** and **244** showed anti-HIV activity ranging from

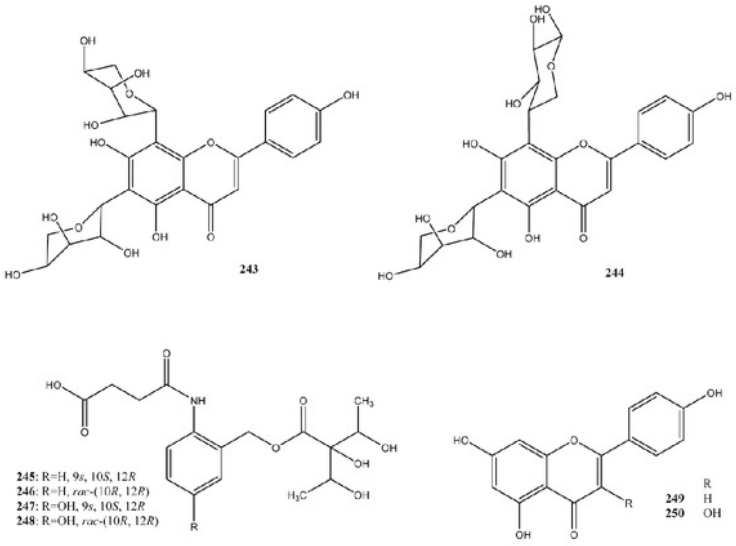

Fig. 10. Isolated Compounds of *Justicia gendarusa*

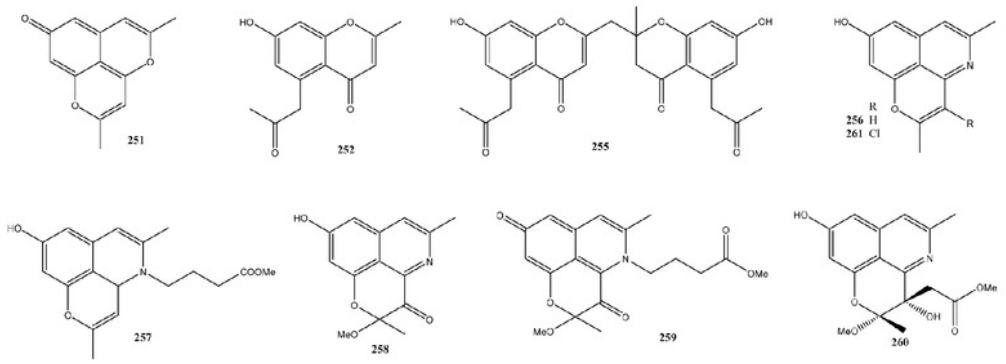

Fig. 11. Isolated Compounds from *Cassia siamea* Leaves

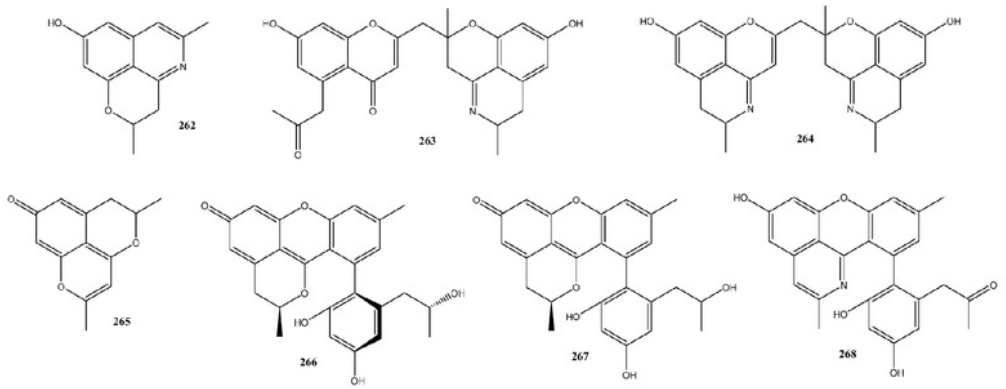

Fig. 12. Isolated Compounds from *Cassia siamea* Flowers

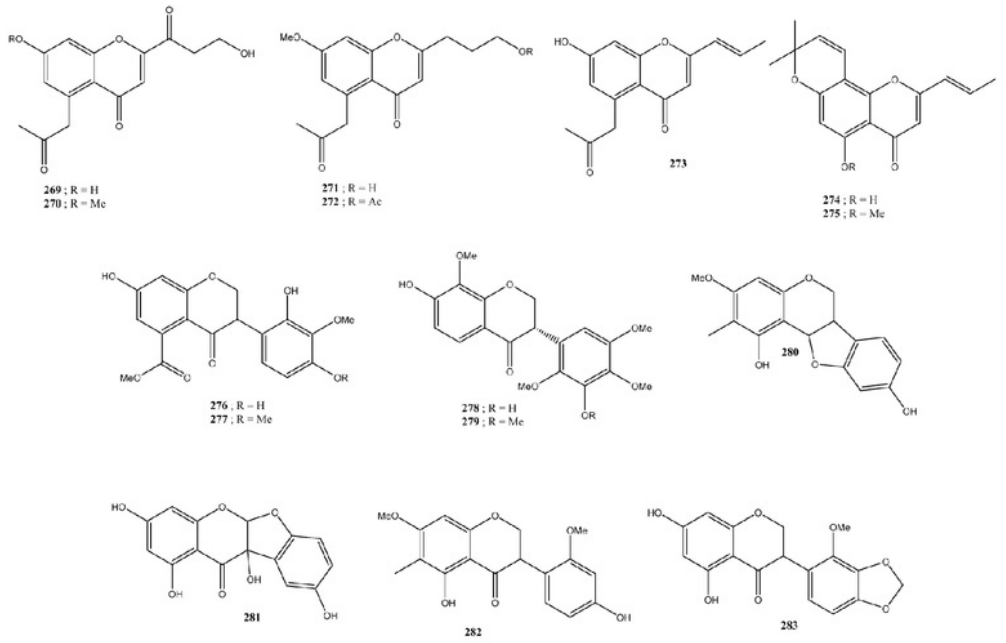

Fig. 13. Isolated Compounds from *Cassia siamea* Stem

1.64 ppm >4.1 ppm, each with barrier values of 0.62×10^6 and 1.4×10^6 cells/mL, respectively.[83] The pharmacokinetic parameters of **243** in human urine after a single oral administration was observed. The result showed an elimination half-life (t 1/2) of **243** in urinary excretion of 4.44±2.14 h, and the rate constant of elimination (Kel) was 0.18±0.07/h.[84]

The 70% ethanol extract of these leaves is not toxic to MOLT-4 cells using a water-soluble tetrazolium-1 (WST-1) assay, with CC_{50} values of 78 μg/mL.[85] The extract of this plant reduced cumulus oophorus dispersibility *in vitro* and testosterone concentration in mouse serum; therefore it may reduce mouse spermatozoa hyaluronidase. A pre-clinical study of an alkaloid free 70% ethanol extract of leaf extract has confirmed its male contraceptive activity.

10. *Cassia siamea*

Cassia siamea (Leguminosae) is traditionally used to treat fever and as an antimalarial. Several chromone derivatives have been isolated, such as anhydrobarakol (**251**),[86] 5-acetonyl-7-hydroxy-2-methylchromone (**252**),[87] 2-methyl-5-propyl-7,12-dihydroxychromone-12-*O*-β-D-glucopyranoside (**253**),[88] and cassiadinine (**254**).[89] In 2008, a new chrobisiamone A (**255**), together with cassiarins A (**256**) and B (**257**) as potent antiplasmodial agents, were found from *Cassia siamea* leaves. The first total synthesis of 253 was done by arenes sequential alkynylation with Sonogashira coupling and 6-endo-dig-cyclization of phenolic oxygens. The seven steps of this reaction yielded 51% alkynes. The compounds **255**, **252**, and **251** inhibited moderate parasite *Plasmodium falciparum* 3D7 with IC_{50} values of 2.6, 4.5 and 7.8 μg/mL, respectively.[41] Other new alkaloids found from the methanol extract were cassiarins G (**258**, 0.0064%), H (**259**, 0.00008%), J (**260**, 0.0022%), and K (**261**, 0.0012%) (Fig. 11). Cassiarin J (**260**) inhibited moderate *P. falciparum* 3D7 (IC_{50} value of 0.3 μM), and **258**, **259**, and **261** (IC_{50} values of >50, >50, 1.4 μM, respectively) were found to be less active than **260**.[91]

Cassiarins A (**256**) is a promising antimalarial drug: it showed powerful effectiveness against *P. falciparum* (IC_{50} 3D7 value of 0.023) and exhibited a high selectivity index (>4348) toward human cell cytotoxicity (IC_{50} MCF7 value of >100).[92] It is also powerful against *P. berghei* mouse malaria, with an ED_{50} value of 0.17 mg/kg.[93]

Six novel cassiarins, C–E (**262**–**264**), 10,11-dihydroanhydrobarakol (**265**),[94] and cassibiphenols A (**266**) and B (**267**)[95] were found from *Cassia siamea* flowers (Fig. 12). Compounds **263** and **264** were dimeric compounds. They dimerized **258** and 5-acetonyl-7-hydroxy-2-methylchromone, then **256** and **262**, respectively. The compounds showed moderate antiplasmodial activity.[96] A new cassiarin F (**268**) (Fig. 12) was isolated from the same part, and displayed potent antiplasmodial activity toward *P. falciparum strain* 3D7 (IC_{50} value of 3.3 μM), yet no cytotoxicity toward HL-60 human blood premyelocytic leukemia (>50 μM).[97]

New chromones of siamchromones A–G (**269**–**275**) were isolated from the stem of this plant. Compound **274** inhibited antitobacco mosaic virus (anti-TMV) activity (35%) with an IC_{50} value of 31.2 μM.[98] Two novel isoflavanones, (3*R*) 7,2′,4′-trihydroxy-3′-methoxy-5-methoxycarbonyl-isoflavanone (**276**) and (3*R*) 7,2′-dihydroxy-3′,4′-dimethoxy-5-methoxycarbonyl-isoflavanone (**277**), along with six known ones, (3*S*)-3′,7-dihydroxy-2′,4′,5′,8-tetramethoxy-isoavan (**278**),[99] (3*S*)-7-hydroxy-2′,3′,4′,5′,8-pentamethoxy-isoavan (**279**),[100] uncinacarpan (**280**),[101] 3,5,7,4′-tetrahydroxy-coumonochromone (**281**),[102] uncinanone E (**282**),[103] and 5,7-dihydroxy-2′-methoxy-3′,4′-methylenedioxy isoavanone (**283**), were isolated from the stems of this plant[104] (Fig. 13). Compounds **276** and **281** displayed potential antiTMV activity, with inhibition rates of 24.6±2.7 and 26.9±2.2%, respectively. In addition, **277**, **278**, **282**, and **283** also showed antiTMV activity, with inhibition rates in the range of 11.8–18.6%.[105]

Conclusion

The effective use of plants or herbs commonly used for Jamu in Indonesia depends on the phytochemical composition of each in relation to the specific biological activity they exhibit. The different phytochemicals identified in the present study have been confirmed to be effective, based on a wide range of biological tests. Zingiberaceae has long been reported to contain several phytochemicals such as terpenoids, flavonoids, phenypropanoids and sesquiterpenes, which participate in a wide variety of bioactivity.

Conflict of Interest The authors declare no conflict of interest.

References

1) Riswan S., Roemantyo H. S., *South Pacific Study*, **23**, 2–10 (2002).
2) Jantan I. B., Yassin M. S. M., Chin C. B., Chen L. L., Sim N. L., *Pharmeur. Bio*, **41**, 392–397 (2003).
3) Banerjee A., Nigam S. S., *Indian J. Med. Res.*, **68**, 864–866 (1978).
4) Ozaki Y., *Chem. Pharm. Bull.*, **38**, 1045–1048 (1990).
5) Gonda R., Tomoda M., Ohara N., Takada K., *Biol. Pharm. Bull.*, **16**, 235–238 (1993).
6) Khar A., Ali A. M., Pardhasaradhi B. V. V., Begum Z., Anjum R., *FEBS Lett.*, **445**, 165–168 (1999).
7) Matsuda H., Morikawa T., Toguchida I., Ninomiya K., Yoshikawa M., *Chem. Pharm. Bull.*, **49**, 1558–1566 (2001).
8) Chirangini P., Sinha S. K., Sharma G. J. J., *Environ. Path. Toxic. Oncol.*, **23**, 235–244 (2004).
9) Lai E. Y., Chyau C. C., Mau J. L., Chen C. C., Lai Y. J., Shih C. F., Lin L. L., *Am. J. Chin. Med.*, **32**, 281–290 (2004).
10) Kamazeri T. S., Samah O. A., Taher M., Susanti D., Qaralleh H., *Asian Pac. J.Trop. Med.*, **5**, 202–209 (2012).
11) Joy P. P., Thomas J., Mathew S., Skaria B. P., "Zingiberaceous medicinal and aromatic plants," Aromatic and Medicinal Plants Research Station, Odakkali, Asamannoor P. O., Kerala, India, 1998, p. 31.
12) Jayaprakasha G. K., Jagan L., Rao M., Sakariah K. K., *Trends Food Sci. Technol.*, **16**, 533–548 (2005).
13) Wang L. Y., Zhang M., Zhang C. F., Wang Z. T., *Biochem. Syst. Ecol.*, **36**, 476–480 (2008).
14) Li S., Yuan W., Deng G., Wang P., Yang P., Aggarwal B. B., *Pharmaceutical Crops*, **2**, 28–54 (2011).
15) Jayaprakasha G. K., Rao L. J. M., Sakariah K. K., *J. Agric. Food Chem.*, **50**, 3668–3672 (2002).
16) Venkateswarlu S., Ramachandra M. S., Subbaraju G. V., *Bioorg. Med. Chem.*, **13**, 6374–6380 (2005).
17) Li W., Wang S., Feng J., Xiao Y., Xue X., Zhang H., Wang Y., Liang X., *Magn. Reson. Chem.*, **47**, 902–908 (2009).
18) Masuda T., Jitoe A., Isobe J., Nakatani N., Yonemori S., *Phytochemistry*, **32**, 1557–1560 (1993).
19) Dao T. T., Nguyen P. H., Won H. K., Kim E. H., Park J., Won B. Y., Oh W. K., *Food Chem.*, **134**, 21–28 (2012).
20) Xiao Y. C., Xie J., Yu M., Liu M., Ran J., Xi Z., Li W., Huang J., *Chin. Chem. Lett.*, **22**, 1457–1460 (2011).

21) Wen J., Qiu T. Y., Yan X. J., Qiu F., *J. Asian Nat. Prod. Res.*, **19**, 1–6 (2017).
22) Yuan T., Zhang C., Qiu C., Xia G., Wang F., Lin B., Li H., Chen L., *Nat. Prod. Res.*, **20**, 1–6 (2017).
23) Friesen R. W., Blouin M., *J. Org. Chem.*, **61**, 7202–7206 (1996).
24) Kamal A., Malik M. S., Azeeza S., Bajee S., Shaik A. A., *Tet. Asym*, **20**, 1267–1271 (2009).
25) Ishii T., Matsuura H., Kaya K., Vairappan C. S., *Biochem. Syst. Ecol.*, **39**, 864–867 (2011).
26) Avanço G. B., Ferreira F. D., Bomfim N. S., Santos P. A. S. R., Peralta R. M., Brugnari T., Mallmann C. A., Filho B. A. A., Mikcha J. M. G., Machinski M. J., *Food Contr.*, **73**, 806–813 (2017).
27) Jiang J., Jin X., Zhang H., Su X., Qiao B., Yuan Y., *J. Pharm. Biomed. Anal.*, **70**, 664–670 (2012).
28) Tanvir E. M., Hossen M. S., Hossain M. F., Afroz R., Gan S. H., Khalil I., Karim N., *J. Food Qual.*, **2017**, 1–8 (2017).
29) Helen M. P. A., Gomathy S. K., Jayasree S., Nizzy A. M., Rajagopal B., Jeeva S., *Asian Pac. J. Trop. Biomed.*, **2**, 637–640 (2012).
30) Jarikasem S., Thubthimthed S., Chawananoraseth K., Suntorntanasat T., "Essential oils from three Curcuma Species collected in Thailand." ed. by Bas, er, Franz G., Cañigueral S., Demirci F., Craker L. E., Gardner Z. E., Chiang Mai, Wocamp III, 2005, pp. 37-41.
31) Akarchariya N., Sirilun S., Julsrigival J., Chansakaowa S., *Asian Pac. J. Trop. Biomed.*, **7**, 881–885 (2017).
32) Oon S. F., Nallappan M., Tee T. T., Shohaimi S., Kassim N. K., Sa'ariwijaya M. S. F., Cheah Y. H., *Cancer Cell Int.*, **15**, 100 (2015).
33) Shiobara Y., Asakawa Y., Kodama M., Takemoto T., *Phytochemistry*, **25**, 1351–1353 (1986).
34) Kawabata J., Tahara S., Mizutani J., *Biol. Chem.*, **45**, 1447–1453 (1981).
35) Friedrich D., Bohlmann F., *Tetrahedron*, **44**, 1369–1392 (1988).
36) Kozhevnikova E. F., Quartararo J., Kozhevnikov I. V., *Appl. Catal. A.*, **245**, 69–78 (2003).
37) Zhang C., Ji J., Ji M., Fan P., *Phytochem. Lett.*, **12**, 215–219 (2015).
38) Zhang C., Fan P., Li M., Lou H., *Helvetica*, **97**, 1295–1300 (2014).
39) Batubaraa I., Julitaa I., Darusmana L. K., Muddathirc A. M., Mitsunagad T., *Procedia Chemistry*, **14**, 216–224 (2015).
40) Salleh N. A. M., Ismail S., Halim M. R. A., *Pharmacognosy Res*, **8**, 309–315 (2016).
41) Kim M., Kim C., Song Y., Hwang J., *Evid. Based Complement. Alternat. Med.*, **2014**, 1–10 (2014).
42) Sirat H. M., Meng L. L., *Malaysian J. Sci.*, **28**, 323–328 (2009).
43) Barr A., *J. Future Med. Chem.*, **2**, 1563–1576 (2010).
44) Diastuti H., Syah Y. M., Juliawaty L. D., Singgih M., *Indo. J. Chem.*, **14**, 32–36 (2014).
45) Sukari M. A., Wah T. S., Saad S. M., Rashid N. Y., Rahmani M., Lajis N., Yun T., Hin X. X., *J. Nat. Prod. Res.*, **24**, 838–845 (2010).
46) Azis S., Tanaka K., Kadota S., Tezuka Y., *J. Nat. Prod.*, **76**, 223–229 (2013).
47) Cho W., Nam J.-W., Kang H.-J., Windono T., Seo E.-K., Lee K.-T., *Int. Immunopharmacol.*, **9**, 1049–1057 (2009).
48) Lakshmi S., Padmaja G., Remani P., *Int. J. Med. Chem.*, **13**, 1–13 (2011).
49) Zhou L., Zhang K., Li J., Cui X., Wang A., Huang S., Zheng S., Lu Y., Chen W., *Reprod. Toxicol.*, **37**, 62–69 (2013).
50) Singh P., Singh S., Kapoor I. P. S., Singh G., Isidorov V., Szczepaniak L., *Food Bioscience*, **3**, 42–48 (2013).
51) Navarro D. F., Souza M. M., Neto R. A., Golin V., Niero R., Yunes R. A., Monache F. D., Filho F. C., *Phytomedicine*, **9**, 427–432 (2002).
52) Rahman S. N. S. A., Wahab N. A., Malek S. N. A., *Evid. Based Complement. Alternat. Med.*, **14**, 1–14 (2013).
53) Jang M. K., Sohn D. H., Ryu J., *Planta Med.*, **67**, 550–552 (2001).
54) Kashara K., Nomura S., Matsuura H., Yamasaki M., Yamato O., Maede Y., Katakura K., Suzuki M., Trimurningsih, Chairul, Yoshihara T., *Planta Med.*, **71**, 482–848 (2005).
55) Azam G., Noman S., Pavel A. M., *Journal of Pharmacognosy and Phytochemistry*, **6**, 171–173 (2017).
56) Reanmongkol W., Subhadhirasakul S., Khaisombat N., Fuengnawakit P., Jantasila S., Khamjun A., *J. Sci. Technol*, **28**, 999–1008 (2006).
57) Suphrom N., Pumthong G., Khorana N., Waranuch N., Limpeanchob N., Ingkaninan K., *Fitoterapi*, **83**, 864–871 (2012).
58) Sirat H. M., Shajarahtunnur J., Hussain J., *Journal of Essential Oil Research*, **10**, 453–458 (1998).
59) Simoh S., Zainal A., *Asian Pac. J. Trop. Biomed.*, **5**, 412–417 (2015).
60) Madhu S. K., Shaukath A. K., Vijayanc V. A., *Acta Trop.*, **113**, 7–11 (2010).
61) Saifudin A., Kadota S., Tezuka Y., *J. Nat. Med.*, **67**, 264–270 (2013).
62) Usia T., Watabe T., Kadota S., Tezuka Y., *Biol. Pharm. Bull.*, **28**, 495–499 (2005).
63) Usia T., Iwata H., Hiratsuka A., Watabe T., Kadota S., Tezuka Y., *J. Nat. Prod.*, **67**, 1079–1083 (2004).
64) Subehan, Usia T., Kadota S., Tezuka Y., *Chem. Pharm. Bull.*, **53**, 333–335 (2005).
65) Zhang S., Liu Q., Liu Y., Qiao H., Liu Y., *Evid. Based Complement. Alternat. Med.*, **2012**, 1–8 (2012).
66) Ling Z., Lv-Yi C., Jing-Yu L., *Chin. J. Nat. Med.*, **10**, 370–373 (2012).
67) Morikawa T., Ando S., Matsuda H., Kataoka S., Muraoka O., Yoshikawa M., *Chem. Pharm. Bull.*, **53**, 625–630 (2005).
68) Ye Y., Li B., *J. Gen. Virol.*, **87**, 2047–2053 (2006).
69) Lathaa C., Shriram V. D., Jahagirdar S. S., Dhakephalkar P. K., Rojatkara S. R., *J. Ethnopharmacol.*, **123**, 522–525 (2009).
70) Ninomiya K., Nishi R., Kamei I., Katsuyama Y., Imagawa T., Chaipech S., Muraoka O., Morikawa T., Manse Y., *Bioorg. Med. Chem.*, **24**, 6215–6224 (2016).
71) Shikha P., Latha P. G., Suja S. R., Anuja G. I., Shyamal S., Shine V. J., Sini S., Kumar N. M., Rajasekaran S., *Indian J. Nat. Prod. Resour.*, **1**, 456–461 (2010).
72) Paval J., Kaitheri S. K., Potu B. K., Govindan S., Kumar R. S., Narayanan S. N., Moorkoth S., *Clinics* (Sao Paulo), **64**, 357–360 (2009).
73) Ayob Z., Samad A. A., Bohari M. S. P., *Sciences and Engineering*, **64**, 45–52 (2013).
74) Krishna K. L., Mruthunjaya K., Patel J. A., *Int. J. Pharmacol.*, **6**, 72–80 (2010).
75) Subramanian N., Jothimanivannan C., Moorthy K., *Asian Journal of Pharmaceutical and Clinical Research*, **5**, 229–233 (2012).
76) Sharma K. K., Saikia K., Kotoky J., Kalita J. C., Devi R., *Int. J. Pharm. Tech. Res.*, **3**, 1635–1640 (2011).
77) Periyanayagam K., Umamaheswari B., Suseela L., Padmini M., Ismail M., *Am. J. Infect. Dis.*, **5**, 187–189 (2009).
78) Krishna K. L., Mehta T. A., Patel J. A., *Pharmacologyonline*, **2**, 9–13 (2010).
79) Prajogo B., Guliet D., Queiroz E_2 F., Wolfender J.-L., Zaini N. C., Hinting A., Hostettmann K., *Folia Medica Indonesia*, **45**, 28–31 (2009).
80) Kiren Y., Deguchi J., Hirasawa Y., Morita H., Prajogo B., *J. Nat. Med.*, **68**, 754–758 (2014).
81) Mnatsakanyan M. M., Queiroz E. F., Marcourt L., Prajogo B., Wolfender J. L., *Planta Med.*, **82**, S1–S381 (2016).
82) Ayob Z., Jamil S., Bohari M. S. P., Ahmad F., Samad A. A., *Sains Malaysiana*, **46**, 457–461 (2017).
83) Prajogo B., Widiyanti P., Nasronudin, Aksana B., *Indonesian Journal of Tropical and Infectious Disease*, **5**, 136–141 (2015).
84) Sihabuddin M., Maria X. X., Flourisa J. S., Pramesti B., Musta'ina S., Radjaram A., Aucky H., Bambang P. E. W., *Journal Medika*

Planta, **1**, 59–68 (2011).
85) Prihartini B., Putu E. H., *Indonesian Journal of Tropical and Infectious Disease*, **6**, 24–28 (2016).
86) Teeyapant R., Srikun O., Wray V., Writte L., *Fitoterapia*, **69**, 475 (1998).
87) Arora S., Deymann H., Tiwri R., Winterfeldt E., *Tetrahedron*, **27**, 981–984 (1971).
88) Lu T., Yi Y., Mao S., Zhou D., Xu Q., Zhang S., *Chin. Chem. Lett.*, **12**, 703 (2001).
89) Biswas K. M., Mallik H., *Phytochemistry*, **25**, 1727–1730 (1986).
90) Oshimi S., Tomizawa Y., Hirasawa Y., Honda T., Ekasari W., Widyawaruyanti A., Rudyanto M., Indrayanto G., Zaini N. C., Morita H., *Bioorg. Med. Chem. Lett.*, **18**, 3761–3763 (2008).
91) Deguchi J., Hirahara T., Hirasawa Y., Ekasari W., Widyawaruyanti A., Shirota O., Shiro M., Morita H., *Chem. Pharm. Bull.*, **60**, 219–222 (2012).
92) Morita H., Tomizawa Y., Deguchi J., Ishikawa T., Arai H., Zaima K., Hosoya T., Hirasawa Y., Matsumoto T., Kamata K., Ekasari W., Widyawaruyanti A., Wahyuni T. S., Zaini N. C., Honda T., *Bioorg. Med. Chem.*, **17**, 8234–8240 (2009).
93) Ekasari W., Widyawaruyanti A., Zaini N. C., Syafruddin D., Honda T., Morita H., *Heterocycles*, **78**, 1831 (2009).
94) Oshimi S., Deguchi J., Hirasawa Y., Ekasari W., Widywawaruyanti A., Wahyuni T. S., Zaini N. C., Shirota O., Morita H., *J. Nat. Prod.*, **72**, 1899–1901 (2009).
95) Deguchi J., Sasaki T., Hirasawa Y., Kaneda T., Kusumawati I., Shirota O., Morita H., *Tetrahedron Lett.*, **55**, 1362–1365 (2014).
96) Oshimi S., Deguchi J., Hirasawa Y., Ekasari W., Widywawaruyanti A., Wahyuni T. S., Zaini N. C., Shirota O., Morita H., *J. Nat. Prod.*, **72**, 1899–1901 (2009).
97) Deguchi J., Hirahara T., Oshimi S., Hirasawa Y., Ekasari W., Shirota O., Honda T., Morita H., *Org. Lett.*, **13**, 4344–4347 (2011).
98) Hu G. F., Zhou B., Gao X. M., Shu L. D., Shent Y., Li G. P., Che C. T., Yang G. Y., *J. Nat. Prod.*, **75**, 1909–1914 (2012).
99) Lane G. A., Newman R. H., *Phytochemistry*, **26**, 295–300 (1986).
100) Alvarez L., Rios M. Y., Esquivel C., Chavez M. I., Delgado G., Aguilar M. I., Villarreal M. L., Navarro V., *J. Nat. Prod.*, **61**, 767–770 (1998).
101) Guchu S. M., Yenesew A., Tsanuo M. K., Gikonyo N. K., Pickett J. A., Hooper A. M., Hassanali A., *Phytochemistry*, **68**, 646–651 (2007).
102) Zhao M., Duan J. A., Che C. T., *Phytochemistry*, **68**, 1471–1479 (2007).
103) Guchu S. M., Yenesew A., Tsanuo M. K., Gikonyo N. K., Pickett J. A., Hooper A. M., Hassanali A., *Phytochemistry*, **68**, 646–651 (2007).
104) Zhao M., Duan J. A., Che C. T., *Phytochemistry*, **68**, 1471–1479 (2007).
105) Hu Q., Niu D., Zhou B., Ye Y., Du G., Meng C., Gao X., *Bull. Korean Chem. Soc.*, **34**, 3013–3016 (2013).

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